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BRIEF COMMUNICATION

Intravenous Infusion System for Chronic Drug Administration in Unrestrained Rats

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GOLDSTEIN, J. M. *Intravenous infusion system for chronic drug administration in unrestrained rats.* PHARMAC. BIOCHEM. BEHAV. 4(5) 613–615, 1976. – This paper describes a system for long-term intravenous infusion studies in relatively unrestrained rats. It has the advantage of allowing continual 24 hr studies to be run without the problems of having the infusion cable tangle or interfere with the normal activity of the rats, and most of the components are either easily made or readily available from commercial sources. The apparatus itself incorporates the features of several reported chronic infusion systems using modifications to produce a feed-through swivel and infusion cable which can be adapted to a wide range of experimental chambers. In addition, a skull implant is described which minimizes the restraining features inherent in harnesses and provides a secure link between the rat and the infusion cable. The implant mates directly with the infusion cable and is readily detachable. The entire system is inexpensive and requires a minimum of construction.

Intravenous infusion Conscious animal Self-administration Swivel

SEVERAL systems for long-term intravenous infusion in unrestrained rats have been described in the literature [2, 4, 5, 6]. Most of the investigators agree that the critical factor involved is to allow freedom to the rat while maintaining a reliable link between the animal and the infusion device. The apparent solution would be to employ some type of swivel arrangement which would allow the rat freedom to move but would prevent the infusion cable from becoming tangled. The construction of various swivels have been described but usually require special parts which must be machined to varying degrees of accuracy thus affording a close fitting watertight device [2, 4, 5, 7, 8]. The use of commercially available swivels could alleviate this problem, but these swivels are usually expensive and require a higher torque to function and rats would have to be fitted with a harness in order to facilitate movement of the swivel [6]. The use of a harness in itself creates a degree of restraint on the rat. Finally, the infusion cable must be constructed in such a way that the rat cannot bite through it. This problem has been handled by either having the animal complete an electrical circuit when it tries to bite the cable, the mild shock deters such a behavior [3], or the infusion cable is protected by a wire covering [1].

The system described in this paper uses an inexpensive commercially available swivel, but with an added arm to reduce the torque, thus allowing an implant rather than a harness to be used. The swivel, infusion cable and implant, which is anchored to the rat's skull, securely attach to each other, but can easily be separated to allow removal of the rat. The system is flexible, no machined parts are required, and the only construction needed (aside from the implant) is to solder the arm to the Tuohy-Borst adapter which is described in the following sections.

DESIGN

Construction of the Implant

The implant is constructed from the base of a 25 ga hypodermic needle (plastic, disposable type), and fitted with a guide cannula (available from Plastic Products Co., Roanoke, Virginia; No. C-313-G). After removal of the needle portion the remaining hub is cut approximately 9 mm from the bottom and a small hole is drilled at a slight angle in the side of the base. The guide cannula is bent at a 45° angle and fitted into the top of the hub so that the shaft of the guide cannula protrudes out of the hole in the base of the hub. The assembly is then inverted and cemented together by pouring the cement into the bottom of the hub. Any fast drying cement may be used, although dental acrylic was found to be the easiest to work with. Before the cement has hardened, a small screw (Star Stainless Screw Co. No. 0/80 × 1/8 in.) is placed head first

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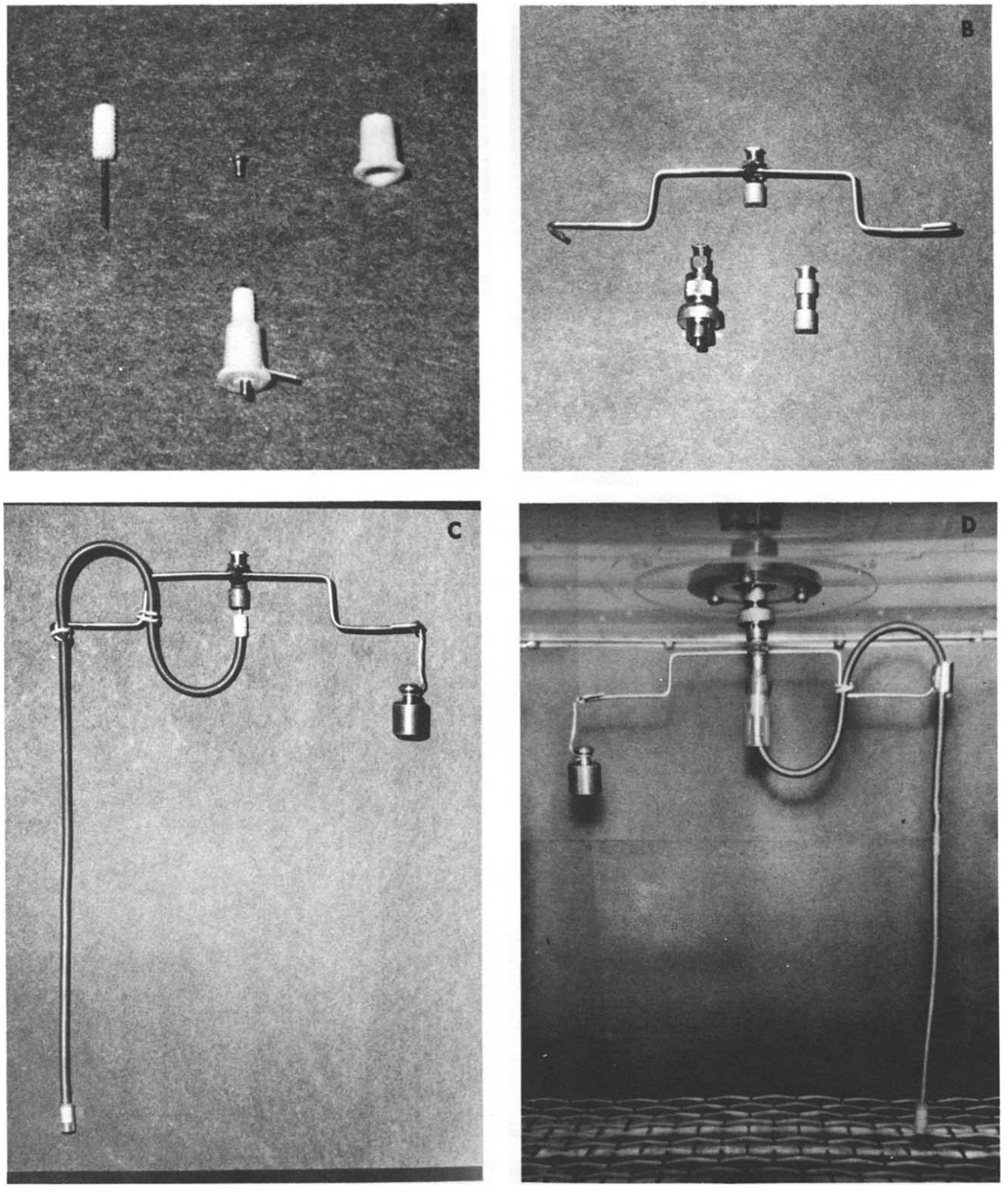

FIG. 1. (A) Components of the implant (guide cannula, mounting screw and needle hub) are shown in the top row, the completed implant is shown on the bottom; (B) The arm is bent according to the picture and the Tuohy-Borst adapter (pictured separately at lower right) is soldered to the arm at its center. The unmounted swivel is pictured in the bottom left; (C) The completed arm assembly is shown with the counterweight mounted on the right and the infusion cable routed around the arm and secured as shown; (D) The swivel has been attached to the arm and mounted on the top of the test chamber using the base of a laboratory accessory stand to secure it. The connection between the Tuohy-Borst adapter and the infusion cable has been reinforced by the addition of a piece of plastic tubing over the connection, and an optional sleeve has been attached to the right side of the arm through which the infusion cable has been routed.

into the base to allow the implant to be screwed into the skull. When the cement has completely dried the guide cannula is bent to almost 90 degrees. The components and completed implant are shown in Fig. 1A. After the external jugular has been cannulated, the catheter is brought subcutaneously to the top of the skull. The implant is then screwed into the bone and acrylic cement is placed around the base to ensure rigid attachment. Prior to cementing, the addition of two screws on either side of the implant will facilitate the adhesion of the acrylic. The end of the catheter is then pushed onto the tip of the guide cannula.

Swivel and Arm Assembly

The swivel (Becton-Dickinson No. 3080-625A) is connected to the arm by means of a Tuohy-Borst adapter (Becton-Dickinson No. 3097-610A). The arm is a thin tube of metal, 6 in. long, which is bent according to the picture in Fig. 1B. The Tuohy-Borst adapter is soldered to the arm at its center. One end of the arm is bent in a small loop to hold the infusion cable, and the other end is attached to a small counterweight (about 20–25 g). The swivel, Tuohy-Borst adapter and completed arm are shown in Fig. 1B.

Infusion Cable

The infusion cable (Plastic Products Company No. C313-C) is available in various lengths with a protective spring covering to prevent the rat from chewing through the cable. A length of 14 in. has been found to be most suitable for a variety of experimental chambers. The cable is attached to the arm by means of the Tuohy-Borst adapter. It is then looped through the end of the arm and the height adjusted for the particular chamber in use. The completed assembly is shown in Fig. 1C.

APPLICATION

The Tuohy-Borst adapter is fitted into the swivel (luerlok connectors facilitate this and provide a leak proof connection) and the swivel is attached by either securing the uppermost stationary portion to the top of the chamber, or using a ring stand and clamp. The infusion cable is attached to the rat by simply screwing it onto the implant. The end of the infusion cable mates with the guide cannula used for the implant, and provides a leakproof seal when screwed down. The rat can easily be taken out by unscrewing the coupling at the end of the infusion cable. When the rat is disconnected from the apparatus, it is advisable to place a dust cap (Plastic Products Co. No. MS-303) over the implant. This will prevent the catheter from becoming clogged. The stationary end of the swivel can be attached to an infusion pump using standard luerlok adapters and polyethylene tubing. The total length of the swivel can be extended by using a needle extension (Becton-Dickinson No. 1118-LLX). Thus the swivel can be extended if the height of the test chamber is a critical factor. Figure 1D shows the infusion system with the swivel mounted on the top of the test chamber.

The infusion system as described above has been in use for several studies in which rats were allowed 24 hr access to self-administration of drugs, 7 days per week including weekends, without any problems with the cable becoming tangled.

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